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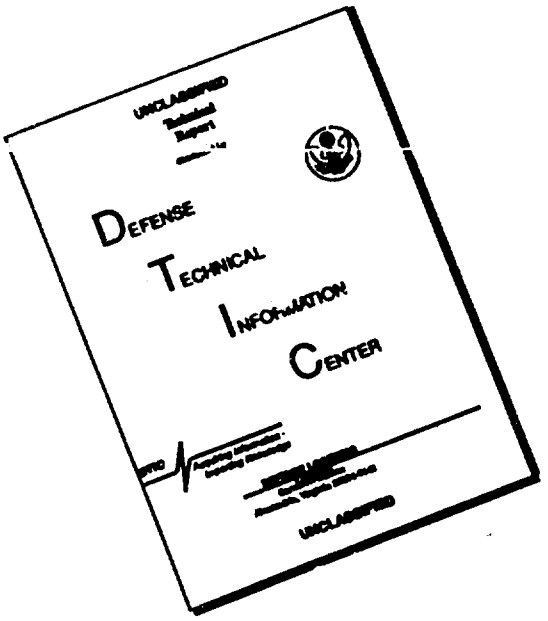

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OUR EXPERIENCE WITH IMMUNOFLUORESCENCE (RELATING TO 250 SERA STUDIED AT THE NANCY DERMATOLOGICAL CLINIC)

Bull. Soc. Franc. Dermatol. Syph.
(Bulletin of the French Society for Dermatology and Syphilis)
Vol 71, 1964, pp 676-678.

J. Beurey, J. Morel and C. Gury

The principle of immunofluorescence, discovered by Coons in 1942, was applied to the diagnosis of syphilis by Deacon, Falcon and Harris in 1957. Borel and Durel were the first to apply this technique in France, and since then many authors have made an effort to specify the mode of execution of this technique and to determine its value (Daguet, Fribourg-Blanc, Thivolet). Our experience, relating to 250 sera, seems to confirm the great importance of the immunofluorescence test [IF] in the diagnosis of syphilis.

Technique

Using the indirect method -- in agreement with all authors -- we carried out quantitative analyses, which made it possible to express the results in the form of a titre, which is the reciprocal of the greatest dilution of the serum which still enables one to see the fluorescent treponemata. We employed a technique which is essentially identical to that of the French authors, and used for antigen, successively, a suspension of the Nicol strain of Treponema pallidum in physiological solution, and a commercial lyophilized antigen, which gave similar labeling. Moreover, we compared an antiglobulin prepared by us and labeled with fluorescein isothiocyanate with a commercial preparation, both of them being diluted 1:20, finding no perceptible difference between the results of the two techniques. The source of UV was a high-pressure mercury vapor lamp (HB) 200). The examination was carried out by means of a dark-ground microscope with a Zeiss BG 12 UV filter.

Value of Test

Each serum was studied both by the classic serological test and by the treponemal immobilization [TPI] test. Right-away the importance of a quantitative determination of the antibodies became evident. This determination, which is difficult to carry out with immobilizing antibodies, is easy to realize with IF. Moreover, in this case the practical problems of carrying out Nelson's test do not present themselves.

But does the IF test possess the qualities of adequate reproducibility, sensitivity and specificity? Let us consider this problem in the light of our experience: the analyses carried out several times in succession showed a satisfactory reproducibility; the sensitivity, compared with that of the TPI is excellent, since we never obtained a negative IF when the Nelson test was positive; a fluorescence at low titers may be observed in undamaged patients which, theoretically, is tantamount to a lack of specificity. This defect requires in practice a titer of greater than 200 to confirm the positivity of a test. As for this titer of 200, it seems to us that it cannot be interpreted in isolation: in effect, among our sera in this case, there are some that belong to known syphilitic patients the course of whose illness was followed, while the others have negative BW and Nelson tests; however, since we have no clinical data about these persons, we cannot prove that they are free from syphilis.

Results Obtained as a Function of the Evolution of the Syphilitic Disease

Primary Syphilis. -- The Nelson test is negative, and the IF is found to be more sensitive even than the classic serological test: in the patients in whom chancre developed in the preserological period (treponema +, BW -), the IF is positive at titers of up to 800. Unfortunately we did not have any observations where the IF was carried out less than seven days after the onset of the chancre. These titers increase rapidly and may attain 12,800 in the serological phase when the TPI test is still negative. The titers most frequently met with in this stage are around 1,600. The institution of treatment entails a slow decrease which culminates in a negative test in a few months. Thus, the titer of the serum of a patient with primary syphilis which had reached 1,600 in May decreased, after a series of 20,000,000 units of penicillin, to 800 in June and 200 in September.

[illegible]ry Syphilis. -- When the classic serological test and t[illegible] test are positive, the IF is always positive. In

this category the titers vary from 200 to 36,000. We may have to do first of all with nontreated secondary syphilis, whose titers range from 6,400 to 36,000, the most frequently encountered titer being 12,000. If the treatment is begun sufficiently early, the titer decreases gradually. If on the other hand it begins at a later stage of the syphilis, the titer maintains itself for a much longer period of time; thus, on the average, the titer is 1,600 in the old, regularly treated cases of syphilis in which the BW and Nelson tests remain positive.

Late, Clinical or Serological Syphilis. At any rate the titer decreases spontaneously even without treatment, and in the old nontreated cases of syphilis without tertiary clinical symptoms the titers are lower: thus, we have observed a syphilitic patient who had exhibited typical clinical lesions of primary and secondary syphilis 25 years ago, who had not received any treatment and who showed an IF of 1,600 without any current pathological symptoms (BW +, Nelson 100%). During the phase of the syphilitic disease in which up to now the Nelson test was the only means of diagnosis, i.e., in the period following the time when the classic serological test becomes negative, IF reveals itself equally valuable: in effect, it also remains positive at titers varying from 200 to 1,600. Better yet, after the total disappearance of reagins and immobilisins, the antibody responsible for the immunofluorescence is frequently still present, in titers ranging from 200 to 800. This confirms the high sensitivity of the test and poses the problem of the origin of this persistent antibody. Do we have to do with the persistence of a slowed-down treponemal activity, as has recently been proved by Collart, Borel and Durel in rabbits with refractory Nelson tests? Or do we have to do simply with the slower disappearance of these fluorescent antibodies? Be that as it may, this high sensitivity of the IF further increases the possibilities of the late diagnosis of syphilis. Our few cases of general paralysis or nontreated tabes exhibit very high titers: 25,000 to 36,000, and in these patients the cephalorrhachidian fluid shows titers of between 1,600 and 4,000. The serum titer decreases during treatment: thus, a case of general paralysis treated since 1948 currently shows a titer of 800, while another case of general paralysis, treated only since 1961, still shows a titer of 4,000. When the IF is negative, the Nelson test is always negative. Here we have to do either with treated syphilitic patients or with undamaged subjects. Among the latter it is possible to find a falsely positive classic serological test: thus, IF, just like the Nelson test, makes it possible to settle the question of these false positives, or at least this is our opinion in the light of the 2,0[illegible] investigated. However, Pages and Many describe (in Oct 19[illegible]) three cases of IF which were falsely positive, while the Nelson test was negative.

Thus the IF is of considerable interest. Nevertheless it is to be regretted that its technique is still not standardized. It can confirm the results of the Nelson test, but in addition -- since it is more easy to perform -- it permits a quantitative determination of the antibodies. Nevertheless, the treponemal immobilization test retains its value: thus, a study of our files shows that in the presence of a 1/200 IF, it is the immobilization test that is alone capable of solving the problem, at least for the time being. The IF is of primary importance for the confirmation of the diagnosis of syphilis in the presence of a chancre in which the treponemata cannot be demonstrated on account of a premature local treatment; and it is said, by some authors, to become positive even before the appearance of a chancre, which would make it possible to effect an early diagnosis in the case of possible contamination. Belatedly, in the evolution of the treated syphilitic disease it permits, in addition, a retrospective diagnosis when all other serological tools fail. This very persistence shows how cautious one must be before definitely stating that the syphilis has been cured.